AMENDMENT UNDER 37 C.F.R. § 1.114(c) Attorney Docket No.: Q94159

U.S. Application No.: 10/574,688

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended): A method for producing aminopyrrolidine derivatives of formula (1), or salts thereof, comprising reaction steps 1 and 2, wherein step 1 is conducted in the presence of one or plural reagents selected from the group consisting of formalin.
paraformaldehyde and trioxane, wherein the indole derivative in reaction step 1 is not substituted at the 3-position in the presence of a synthon of formaldehyde and wherein reaction step 2 is unnecessary if both R¹ and R² are hydrogen:

Attorney Docket No.: Q94159

AMENDMENT UNDER 37 C.F.R. § 1.114(c) U.S. Application No.: 10/574,688

wherein

 R^1 and R^2 represent independently hydrogen or a protecting group for amino group (wherein R^1 and R^2 may, taken together, form a cyclic structure);

R3 represents hydrogen or C1-C6 alkyl;

R11 represents hydrogen, C1-C6 alkyl or C2-C7 alkanoyl;

 R^{12} , R^{14} , R^{15} , R^{16} and R^{17} represent independently hydrogen, halogen, optionally halogenated C_1 – C_6 alkvl, optionally halogenated C_1 – C_6 alkvy, hydroxyl or C_2 – C_7

alkoxycarbonyl; and

 R^{23} , R^{24} , R^{25} and R^{26} represent independently hydrogen, halogen, optionally halogenated C_1 – C_6 alkvl. optionally halogenated C_1 – C_6 alkvv. or hydroxyl; and

wherein the synthon of formaldehydethe reagent is at least one selected from the group consisting of formalin, paraformaldehyde and trioxane.

- 2. (original): The production method according to claim 1, wherein the protecting group for amino group as R¹ or R² is methoxycarbonyl, t-butoxycarbonyl, benzyloxycarbonyl, allyloxycarbonyl, formyl, acetyl, benzoyl, methyl, ethyl, allyl, benzenesulfonyl or phthaloyl, wherein, when said protecting group for amino group contains an aromatic ring, the aromatic ring may be optionally substituted with one or more of nitro, amino, C₁–C₆ alkyl, C₁–C₆ alkoxy or halogen.
- (original): The production method according to claim 1, wherein either of R¹ and R² is hydrogen and the other is t-butoxycarbonyl.
 - 4-6. (canceled).

Attorney Docket No.: Q94159

AMENDMENT UNDER 37 C.F.R. § 1.114(c) U.S. Application No.: 10/574,688

- 7. **(previously presented):** The production method according to claim 1, wherein reaction step 2 is removal of the protection group for the amino group by acid hydrolysis.
- (previously presented): The production method according to claim 1, wherein reaction step 2 involves treatment with hydrogen chloride in organic solvent.
- 9. (currently amended): A method for producing aminopyrrolidine derivatives or salts thereof, comprising a condensation step represented by the following reaction formula (II), wherein the condensation step is performed by treatment with an anthranilic acid derivative in amixed solvent of aprotic solvent and C₁₋₃ alcohol in the presence of a condensing agent:

m

wherein

R3 represents hydrogen-or C1-C6-alkyl;

R11 represents hydrogen, C1-C6-alkyl or C2-C7 alkanoyl;

R¹², R¹⁴-and R¹⁵ represent independently hydrogen;

R16 represents hydrogen or a methyl group; and

 R^{17} represent-represents independently hydrogen, halogen, optionally halogenated C_1 - C_6 alkyl, optionally halogenated C_1 - C_6 alkoxy, hydroxyl or C_2 - C_7 alkoxycarbonyl; and

 R^{23} , R^{24} , R^{26} and R^{26} represent independently hydrogen, halogen, optionally halogenated C_4 – C_6 alkyl, optionally halogenated C_4 – C_6 alkyl, optionally halogenated C_4 – C_6 alkyl, optionally halogenated C_4 – C_6 alkows or hydroxyl; and

R²⁵ represents a trifluoromethoxy group.

- 10. (original): The production method according to claim 9, wherein the condensing agent is one or more of a compound selected from 1,3-dicyclohexylcarbodiimide, isobutyl chloroformate, pivaloyl chloride, isovaleryl chloride, 1-ethyl-3-(3-dimethylamino-propyl)carbodiimide, 1-cyclohexyl-3-morpholinoethylcarbodiimide, 1-cyclohexyl-3-(4-diethylaminocyclohexyl)carboximide, N,N-carbonyldiimidazole and 2-chloro-1,3-dimethylimidazolinium chloride.
- (original): The production method according to claim 9, wherein the condensing agent is 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride.

12. (previously presented): The production method according to claim 9, wherein, in said condensation step, are additionally used one or more of an additive selected from *p*-nitrophenol, hydroxysuccinimide, hydroxyphthalimide, 1-hydroxy-1,2,3-benzotriazole, 3-hydroxy-4-oxo-3,4-dihydro-1,2,3-benzotriazine, *N*-hydroxy-5-norbomene-2,3-dicarboximide and ethyl 2-hydroxyimino-2-cyanoacetate.

- (previously presented): The production method according to claim 9, wherein, in said condensation step, 1-hydroxy-1.2.3-benzotriazole is additionally used as an additive.
- (previously presented): The production method according to claim 9, wherein, in said condensation step, triethylamine is additionally used.
- 15. (previously presented): The production method according to claim 9, which further comprises a deprotection step represented by the following reaction step 4:

Attorney Docket No.: Q94159

AMENDMENT UNDER 37 C.F.R. § 1.114(c) U.S. Application No.: 10/574,688

wherein R^3 , R^{11} , R^{12} , R^{14} , R^{15} , R^{16} , R^{17} , R^{23} , R^{24} , R^{25} and R^{26} are as defined in reaction formula (ID);

 R^5 and R^6 represent independently hydrogen or a protecting group for amino group (wherein R^5 and R^6 may, taken together, form a cyclic structure) except for the case where R^5 and R^6 are simultaneously hydrogen.

16. (original): The production method according to claim 15, wherein said reaction step 4 involves treatment with hydrogen chloride in organic solvent.

17. (previously presented): The production method according to claim 15, which further comprises an introduction step of an indole derivative represented by reaction step 3:

AMENDMENT UNDER 37 C.F.R. § 1.114(c) U.S. Application No.: 10/574,688

HN
$$\stackrel{\circ}{\underset{\mathsf{R}^3}{\bigvee}} \overset{\circ}{\underset{\mathsf{R}^6}{\bigvee}} \overset{\circ}{\underset{\mathsf{R}^6}{\bigvee}}$$

reaction step 4

wherein R³, R⁵, R⁶, R¹¹, R¹², R¹⁴, R¹⁵, R¹⁶, R¹⁷, R²³, R²⁴, R²⁵ and R²⁶ are as defined above.

18. (currently amended): The production method according to claim 17, wherein said reaction step 3 is reaction of an indole derivative having no substituent at the 3-position in the presence of a synthon of formaldehydeone or plural reagents selected from the group consisting of formalin, paraformaldehyde and trioxane.

- (currently amended): The production method according to claim 18, wherein the synthon-of-formaldehydercagent is formalin.
- 20. (original): The production method according to claim 17, wherein said reaction step 3 is reaction of an indole derivative substituted with a dialkylaminomethyl group at the 3position.
- 21. (previously presented): The production method according to claim 17, which further comprises a removal step of a benzyl group represented by the following reaction step 2:

reaction step 2

HN
$$R^3$$

reaction step 2

 R^{16}
 R^{16}
 R^{16}
 R^{16}
 R^{16}
 R^{16}

reaction step 3

 R^{16}
 $R^{$

wherein R³, R⁵, R⁶, R¹¹, R¹², R¹⁴, R¹⁵, R¹⁶, R¹⁷, R²³, R²⁴, R²⁵ and R²⁶ are as defined above.

22. (original): The production method according to claim 21, wherein, in said reaction step 2, a hydrogen source is used in the presence of palladium catalyst.

- 23. (original): The production method according to claim 22, wherein the hydrogen source is gaseous hydrogen.
- 24. (previously presented): The production method according to claim 21, which further comprises a condensation step with an amino acid derivative represented by the following reaction step 1:

wherein R³, R⁵, R⁶, R¹¹, R¹², R¹⁴, R¹⁵, R¹⁶, R¹⁷, R²³, R²⁴, R²⁵ and R²⁶ are as defined above.

25. (original): The production method according to claim 24, wherein, in said reaction step 1, are used one or more of a condensing agent selected from 1,3-dicyclohexylcarbodiimide, isobutyl chloroformate, pivaloyl chloride, isovaleryl chloride, 1-ethyl-3-(3-dimethylamino-propyl)carbodiimide, 1-cyclohexyl-3-morpholinoethylcarbodiimide, 1-cyclohexyl-3-(4-diethylaminocyclohexyl)carboximide, N,N-carbonyldiimidazole and 2-chloro-1,3-dimethylimidazolinium chloride.

- 26. (original): The production method according to claim 24, wherein, in said reaction step 1, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide is used as a condensing agent.
- 27. (previously presented): The production method according to claim 24, wherein, in said reaction step 1, are additionally used one or more of an additive selected from p-nitrophenol, hydroxysuccinimide, hydroxyphthalimide, 1-hydroxy-1,2,3-benzotriazole, 3-hydroxy-4-oxo-3,4-dihydro-1,2,3-benzotriazine, N-hydroxy-5-norbornene-2,3-dicarboximide and ethyl 2-hydroxyimino-2-cyanoacetate.
- 28. (previously presented): The production method according to claim 24, wherein, in said reaction step 1, 1-hydroxy-1,2,3-benzotriazole is additionally used as an additive.
- 29. (previously presented): The production method according to claim 24, wherein, in said reaction step 1, triethylamine is additionally used.

30. (previously presented): The production method according to claim 15, wherein the protecting group for amino group as R^5 and R^6 is methoxycarbonyl, t-butoxycarbonyl, benzyloxycarbonyl, allyloxycarbonyl, formyl, acetyl, benzoyl, methyl, ethyl, allyl, benzenesulfonyl or phthaloyl, wherein, when said protecting group for the amino group contains an aromatic ring, the aromatic ring may be optionally substituted with one or more of nitro, amino, $C_1 - C_6$ alkyl, $C_1 - C_6$ alkyoy or halogen.

- 31. (previously presented): The production method according to claim 15, wherein either of R⁵ and R⁶ is hydrogen and the other is t-butoxycarbonyl.
- 32. (previously presented): The production method according to claim 1, wherein R³ is hydrogen.
- 33. (previously presented): The production method according to claim 1, wherein R^{11} , R^{12} , R^{14} , R^{15} and R^{17} are all hydrogen.
- $\textbf{34.} \qquad \textbf{(previously presented):} \ The production method according to claim 1, wherein \\ R^{16} \ is methyl.$

35. (previously presented): The production method according to claim 1, wherein R^{23} . R^{24} and R^{26} are all hydrogen.

36. (previously presented): The production method according to claim 1, wherein R^{25} is trifluoromethoxy.

37-52. (canceled).

53. (previously presented): A method for producing aminopyrrolidine derivatives of formula (I), or salts thereof, comprising reaction steps 1 and 2, wherein the indole derivative in reaction step 1 has a dialkylaminomethyl group at the 3-position and wherein reaction step 2 is unnecessary if both R¹ and R² are hydrogen:

wherein

 R^1 and R^2 represent independently hydrogen or a protecting group for amino group (wherein R^1 and R^2 may, taken together, form a cyclic structure);

R³ represents hydrogen or C₁-C₆ alkyl;

R¹¹ represents hydrogen, C₁-C₆ alkyl or C₂-C₇ alkanoyl;

 R^{12} , R^{14} , R^{15} , R^{16} and R^{17} represent independently hydrogen, halogen, optionally halogenated C_1 – C_6 alkoxy, hydroxyl or C_2 – C_7 alkoxycarbonyl; and

R²³, R²⁴, R²⁵ and R²⁶ represent independently hydrogen, halogen, optionally halogenated
C₁-C₆ alkyl, optionally halogenated C₁-C₆ alkoxy or hydroxyl.

- 54. (previously presented): The production method according to claim 53, wherein the protecting group for amino group as R^1 or R^2 is methoxycarbonyl, *t*-butoxycarbonyl, benzyloxycarbonyl, allyloxycarbonyl, formyl, acetyl, benzoyl, methyl, ethyl, allyl, benzenesulfonyl or phthaloyl, wherein, when said protecting group for amino group contains an aromatic ring, the aromatic ring may be optionally substituted with one or more of nitro, amino, C_1 – C_6 alkyl, C_1 – C_6 alkyl, C_1 – C_6 alkyoxy or halogen.
- 55. (previously presented): The production method according to claim 53, wherein either of \mathbb{R}^1 and \mathbb{R}^2 is hydrogen and the other is t-butoxycarbonyl.
- 56. (previously presented): The production method according to claim 53, wherein reaction step 2 is removal of the protection group for the amino group by acid hydrolysis.
- **57. (previously presented):** The production method according to claim 53, wherein reaction step 2 involves treatment with hydrogen chloride in organic solvent.